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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/718,717	11/22/2000	Aya Jakobovits	ABGX-001CON3	5842
24353	7590	06/15/2004	EXAMINER	
BOZICEVIC, FIELD & FRANCIS LLP 200 MIDDLEFIELD RD SUITE 200 MENLO PARK, CA 94025			MCKELVEY, TERRY ALAN	
			ART UNIT	PAPER NUMBER
			1636	

DATE MAILED: 06/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

3.11

Office Action Summary	Application No. 09/718,717	Applicant(s) JAKOBOVITS ET AL.	
	Examiner Terry A. McKelvey	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 March 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2-7, 11 and 12 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 11 and 12 is/are allowed.
- 6) ☒ Claim(s) 2-7 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

All objections and rejections not repeated in the instant Action have been withdrawn due to applicant's response to the previous Action.

Claim Rejections - 35 USC § 112

Claims 2-7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making a mammalian cell having about a 55 kb deletion, does not reasonably provide enablement for making a deletion in the entire range of 50 kb to 3000 kb. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. This rejection is maintained for reasons of record set forth in papers mailed 9/7/01, 6/26/02, and 9/23/03. Applicants' arguments filed 3/22/04 have been fully considered but they are not deemed to be persuasive.

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Response to Arguments

The applicant argues that the instant specification provides ample guidance for one of skill in the art to practice the invention without undue experimentation. This argument is not persuasive because the guidance is merely the general teachings like that in the prior art for doing deletions using a replacement targeting construct and positive selection. There is nothing in the guidance of the instant application that specifically teaches how to predictably obtain the deletions in the range of up to 3000 kb. The single working example is at the very low end of the range. There is nothing in either the guidance in the specification or the working example in the specification which teaches how to overcome the art-recognized unpredictability of making very large deletions using a replacement targeting construct and positive selection, much larger than the mere 55 kb deletion made in the working example.

The applicant argues that the only experiments, if any, that need be performed to enable the entire scope of the claim are those designed to create a construct having the recited features, and to determine whether a cell population includes a genomic deletion in the recited size range, which are readily accomplished through routine experimentation. This argument is not persuasive because if the skilled artisan follows the

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generic guidance presented by the application, which does not appreciably differ from the prior art, but fails to obtain cells having deletion in the range as claimed, one or an unknown number more rounds of unpredictable experimentation, involving unpredictable changes to the generic method neither taught nor suggested by the prior art or the specification, would be required before the full scope of the claimed methods could be practiced. This is likely for the full scope of the claimed invention given the unpredictability in the art as set forth in the rejection of record, and especially detailed in pages 3-8 of the paper mailed 9/23/03. This would be considered to be inventive activity since it would require trying unpredictable changes that go beyond the generic teachings in the prior art and in the specification in order to achieve the full scope of the claimed invention. There is no evidence of record that the unpredictability in the art that is specifically taught by several references concerning making large deletions using the claimed method is overcome by the instant application so that the full claimed scope could be practiced using only routine experimentation. This is highlighted by the fact that the applicant has not and cannot point to any guidance that is beyond what the prior art teaches and which would make the full

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scope of the claimed invention achievable by mere routine experimentation.

The applicant argues that the instant specification provides guidance that the homologous sequences in the construct are at least about 500 base pairs. However, this argument about guidance is not persuasive because there is no evidence that having homologous sequences of at least about 500 base pairs predictably can result in the huge deletions as claimed. The only evidence for any large deletion based upon the guidance is the single working example of a 55 kb deletion, which can only be said to be representative of the very lowest end of the claimed scope of from about 50 kb to about 3000 kb. There is nothing in the guidance that is directed to making the largest deletions in the rest of the claimed range which multiple references of the prior art teach are unpredictable.

The applicant argues that the specification need not contain a working example if the invention is otherwise disclosed in such a manner that one skilled in the art would be able to practice the invention without undue experimentation, and nevertheless the specification does provide a working example. This argument is not persuasive because there are multiple references in the prior art which teaches the same method, but indicates that the larger ranges of deletion are

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unable and unpredictable to be achieved. As indicated above, there is no teaching in the instant application which teaches how to predictably overcome the failures of the prior art so as to achieve the full scope of the claimed invention. Thus, the specification is not otherwise disclosed in such a manner that one skilled in the art would be able to practice the invention without undue experimentation because unpredictable experimentation would be required to overcome the deficiencies in the prior art which are in no way remedied by the instant application.

The applicant argues that the skill level of the artisan in the art is high. That is true, but this fact in no way relates to overcoming art-recognized failures and unpredictability in achieving large deletions using the method taught in the prior art for much smaller deletions, which is essentially taught by the instant application, but indicated by the applicant as being usable for making deletions about sixty times (or more) larger than that achieved by either the prior art or by the single working example taught in the specification.

The applicant argues that the courts have clearly taught that the specification does not have to disclose every species of a genus that would work and every species that would not work. This argument is not persuasive in the instant case

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because the prior art readily teaches the unpredictability in obtaining very large deletions using the claimed method. The instant application teaches and shows that a slightly larger deletion than the best prior art deletion can be made, about twice as large. This scope is supported by the teachings of the instant application. However, the unpredictability of making the much larger deletions that are also being claimed remains. The applicant has not addressed the unpredictability in the prior art in the instant response at all. The teachings of Ramirez-Solis, Brenner et al, and Bradley et al, cited in the last action, all of which teach the unpredictability of making the much larger deletions, were not addressed by the applicant and thus the applicant's arguments concerning unpredictability in the art are not persuasive. Every species of the claimed genus is not being required to be disclosed, but instead the scope of the claimed invention must be commensurate with the enabled teachings of the claimed invention. As demonstrated by the arguments above, this is not the case with the instant invention. Simply making one deletion that is only about twice the size of prior art deletions in the absence of any other specific teachings to show the predictability of making even larger deletions does not support the enablement of making

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deletions that are about 150 times larger than the prior art deletions.

Therefore, in light of all available evidence, including the rejection set forth in the previous Office Actions, maintained above, the applicant's arguments, and the arguments set forth above and in the previous Office Actions, the claimed invention is still not considered to be enabled for the full, claimed scope and thus the rejection under 35 USC paragraph is properly maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

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however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is 703-872-9306. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning rejections or other major issues in this communication or earlier communications from the examiner should be directed to Terry A. McKelvey whose telephone number is (571) 272-0775. The examiner can normally be reached on Monday through Friday, except for Wednesdays, from about 7:30 AM to about 6:00 PM. A phone message left at this number will be responded to as soon as possible (i.e., shortly after the examiner returns to his office).

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel can be reached on (571) 272-0781.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.



Terry A. McKelvey, Ph.D.
Primary Examiner
Art Unit 1636

June 14, 2004